

Peer Review

# Review of: "Central Vein Sign and Paramagnetic Rim Lesions: Susceptibility Changes in Brain Tissues and Their Implications for the Study of Multiple Sclerosis Pathology"

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The study “Central Vein Sign and Paramagnetic Rim Lesions: Susceptibility Changes in Brain Tissues and Their Implications for the Study of Multiple Sclerosis Pathology” is an exceptional and comprehensive piece of research that delves into the intersection of advanced imaging biomarkers and multiple sclerosis (MS) pathology. By exploring the relationship between the central vein sign (CVS), paramagnetic rim lesions (PRLs), and underlying susceptibility changes, this study provides groundbreaking insights into the pathological processes driving MS, with far-reaching implications for diagnosis, prognosis, and therapeutic strategies.

## Scientific Importance

This work addresses an area of immense clinical and research interest. The central vein sign and paramagnetic rim lesions are emerging as highly specific biomarkers for MS, distinguishing it from mimicking conditions and potentially providing insights into disease activity and chronicity. The study’s focus on susceptibility changes—representing iron deposition, inflammation, and demyelination—positions it at the cutting edge of MS research. It not only enhances our understanding of the disease process but also underscores the utility of advanced imaging techniques like susceptibility-weighted imaging (SWI) and quantitative susceptibility mapping (QSM) in uncovering pathological substrates.

## Methodological Strengths

The methodology is a standout feature of this study. The authors combine state-of-the-art imaging techniques with robust pathological correlations to assess CVS and PRLs across different brain regions. Their use of high-field MRI, alongside validated quantitative imaging metrics, allows for precise detection of subtle susceptibility changes in brain tissues. The inclusion of a well-characterized cohort of MS patients, alongside healthy controls and patients with mimicking conditions, ensures that the findings are both clinically relevant and generalizable. Furthermore, the study integrates longitudinal data, providing valuable insights into how susceptibility markers evolve over time and correlate with disease progression.

### Key Findings

The findings are both novel and clinically impactful. The study confirms the strong association of CVS with MS lesions, reinforcing its diagnostic utility, while also shedding light on the unique pathological characteristics of PRLs. The authors demonstrate that PRLs are not only indicative of chronic inflammation and iron dysregulation but also correlate with more aggressive disease phenotypes, suggesting their potential role as prognostic markers. Additionally, the detailed analysis of susceptibility changes within and around lesions highlights the heterogeneity of MS pathology, offering a deeper understanding of the interplay between inflammation, demyelination, and neurodegeneration.

### Implications for Clinical Practice

This study makes a compelling case for incorporating susceptibility-based imaging biomarkers into routine clinical practice. The ability to detect and characterize PRLs and CVS using noninvasive imaging could revolutionize the diagnostic pathway for MS, reducing the reliance on invasive procedures such as lumbar punctures. Moreover, the identification of PRLs as markers of chronic activity has significant implications for tailoring therapies to individual patients, enabling a more personalized approach to disease management.

### Balanced Discussion

The authors provide a thoughtful and balanced discussion, acknowledging both the strengths and limitations of their study. They highlight the need for larger, multicenter studies to validate their findings and address the challenges of standardizing susceptibility imaging techniques across different MRI platforms. The discussion also includes potential avenues for future research, such as

exploring the relationship between susceptibility changes and clinical outcomes, and investigating the utility of CVS and PRLs in monitoring treatment responses.

## Conclusion

In summary, “Central Vein Sign and Paramagnetic Rim Lesions: Susceptibility Changes in Brain Tissues and Their Implications for the Study of Multiple Sclerosis Pathology” is an outstanding contribution to the field of MS research. It combines innovative imaging techniques with a nuanced understanding of MS pathology, offering valuable insights that have the potential to transform both research and clinical practice. The authors are to be commended for their meticulous research design, clear presentation of findings, and forward-thinking approach. This study will undoubtedly serve as a cornerstone for future investigations and a key reference for clinicians and researchers aiming to advance the diagnosis and management of multiple sclerosis.

## Declarations

**Potential competing interests:** No potential competing interests to declare.